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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,117	01/16/2001	Raju S.K. Chaganti	43771-A-PCT-US-Y/JPW/EMW	3093

7590 12/02/2002

Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/02/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/761,117	CHAGANTI ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-55* is/are pending in the application.

4a) Of the above claim(s) *47-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *47-55* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment filed September 16, 2002 (Paper No. 11) has been entered. Claims 46-55 are pending. Claims 47-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9. Claim 46 is being examined. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

New formal matters, objections, and/or rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to or encompass a method of determining whether a subject has non-Hodgkin's lymphoma by incubating a suitable body fluid from the patient with an antibody that

binds a polypeptide having the amino acid sequence of SEQ ID NO: 2. SEQ ID NO: 2 is the amino acid sequence of BCL-6 (the present specification at page 7, lines 30-31). The BCL-6 protein is a nuclear phosphoprotein belonging to the POZ/Zinc finger (ZF) family of transcription factors. BCL-6 functions as a potent transcriptional repressor by binding to its DNA target sequence. See Dalla-Favera (a12), page 25, paragraph 0380. The plasma membrane provides the basic structure of the cell membrane and serves as a relatively impermeable barrier to the passage of most water-soluble molecules. See Alberts (u12), page 477, first paragraph, through paragraph bridging pages 477-478. The present specification does describe or teach, or provide working examples of, getting an antibody molecule bound to a solid support across a relatively impermeable barrier such that the antibody is able to bind its intended target, which is an intracellular nuclear phosphoprotein. There is nothing in the present specification to indicate that SEQ ID NO: 2 is secreted from the cell such that it would be present in a sample of suitable body fluid. Further, BCL-6 is expressed in both normal and neoplastic B-cells. See Onizuka (v12) at page 28, paragraph bridging left and right columns. The specification lacks guidance for distinguishing normal and neoplastic BCL-6 expression such that an indication of non-Hodgkin's lymphoma would occur. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Lysis of the cells in the suitable body fluid, critical or essential to the practice of

the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Lysis of the cells is critical or essential to the practice of the invention because the BCL-6 protein is a nuclear protein (see Dalla-Favera (a12), page 25, paragraph 0380), and the plasma membrane serves as a relatively impermeable barrier to the passage of most water-soluble molecules (see Alberts (u12), page 477, first paragraph, through paragraph bridging pages 477-478). Lysis of the cells is not enabled by the disclosure because the present specification does describe or teach, or provide working examples of, getting an antibody molecule bound to a solid support across a relatively impermeable barrier such that the antibody is able to bind its intended target, which is an intracellular nuclear phosphoprotein. There is nothing in the present specification to indicate that SEQ ID NO: 2 is secreted from the cell such that it would be present in a sample of suitable body fluid.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass a method of determining whether a subject has non-Hodgkin's lymphoma by incubating a suitable body fluid from the patient with an antibody that binds a polypeptide having the amino acid sequence of SEQ ID NO: 2. SEQ ID NO: 2 is the amino acid sequence of BCL-6 (page 7, lines 30-31). The BCL-6 protein is a nuclear phosphoprotein belonging to the POZ/Zinc finger (ZF) family of transcription factors. BCL-6 functions as a potent transcriptional repressor by binding to its DNA target sequence. See Dalla-Favera (a12), page 25, paragraph 0380. The plasma membrane provides the basic

structure of the cell membrane and serves as a relatively impermeable barrier to the passage of most water-soluble molecules. See Alberts (u12), page 477, first paragraph, through paragraph bridging pages 477-478. The present specification does describe or teach, or provide working examples of, getting an antibody molecule bound to a solid support across a relatively impermeable barrier such that the antibody is able to bind its intended target, which is an intracellular nuclear phosphoprotein. There is nothing in the present specification to indicate that SEQ ID NO: 2 is secreted from the cell such that it would be present in a sample of suitable body fluid. Further, BCL-6 is expressed in both normal and neoplastic B-cells. See Onizuka (v12) at page 28, paragraph bridging left and right columns. The specification lacks guidance for distinguishing normal and neoplastic BCL-6 expression such that an indication of non-Hodgkin's lymphoma would occur. The claimed invention is not representative of disclosure because there is no express, inherent, or implicit support for the claim as a whole such that the invention will operate as intended. Therefore, Applicant was not in possession of the necessary attributes required by the claimed invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amended claim raises the issue of new matter because the claimed invention is not representative of disclosure. The claimed invention is not representative of disclosure because there is no express, inherent, or implicit support for the claimed method as a whole.

Conclusion

Claim 46 is not allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

If submitting official correspondence by fax, applicants are encouraged to submit official correspondence to the following TC 1600 Before and After Final RightFax numbers:

Before Final (703) 872-9306

After Final (703) 872-9307

In addition to the Official RightFax numbers above, the TC 1600 Fax Center has the following Official Fax numbers: (703) 305-3592, (703) 308-4242 and (703) 305-3014.

Customers are also advised to use Certificate of Facsimile procedures when submitting a reply to a non-final or final Office action by facsimile (see 37 CFR 1.6 and 1.8).

Faxed draft or informal communications should be directed to the examiner at (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David Romeo
David Romeo
Primary Examiner
Art Unit 1647

DSR
November 30, 2002

#11D
DmT
9-24-02

Dkt. 43771-AZY-PCT-US/JPW/AJM/AG

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Riccardo Dalla-Favera, et al.

Serial No.: 09/761,117 Examiner: David S. Romeo

Filed : January 16, 2001 Group Art Unit: 1647

For : CLONING AND USES OF THE GENETIC LOCUS bcl-6

1185 Avenue of the Americas
New York, New York 10036
September 9, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT IN RESPONSE TO APRIL 8, 2002 OFFICE ACTION AND PETITION FOR A TWO-MONTH EXTENSION OF TIME

This Amendment is submitted in response to an April 8, 2002 Office Action issued by the United States Patent and Trademark Office in connection with the above-identified application. A response to the April 8, 2002 Office Action was originally due July 8, 2002. Applicants hereby petition for a two-month extension of time. Applicants have previously established small entity status. The required fee for a two-month extension of time for a small entity is $200.00 and a check for this amount is enclosed. Therefore, a response to the April 8, 2002 Office Action is now due September 8, 2002. However, since September 8, 2002 falls on a Sunday, a response filed on the next business day, i.e. Monday, September 9, 2002, shall be considered timely. Accordingly, this Amendment is being timely filed.

Please amend the subject application as follows:

In the Claims:

46. (Amended) An assay for determining whether a subject has non-Hodgkins lymphoma comprising:

(a) incubating a sample of suitable body fluid from the subject with an antibody that binds to a polypeptide having the sequence set forth in SEQ ID NO:2, wherein the antibody is bound to a solid support;

D1

(b) separating the sample from the support; and

(c) determining whether the polypeptide is bound to the antibody, the presence of polypeptide bound to the antibody indicating that the subject has non-Hodgkins lymphoma.

REMARKS

Claim 46-55 are pending in the subject application. Claim 47-55 are withdrawn. Claim 46 is under examination. By this Amendment, applicants have amended claim 46 to make certain minor changes. Accordingly, claim 46 is still under examination in the subject application.

Support for the addition of "polypeptide having the sequence set forth in SEQ ID NO:2" can be found, *inter alia*, at page 7, lines 30-31 of the specification. Applicants maintain that the changes to claim 46 raise no issue of new matter.

A marked up version of the amended claim is attached hereto as **Exhibit A**, pursuant to the requirements of 37 C.F.R. §1.121.

Marked-Up Version of Amended Claim:

46. (Amended) An assay for determining whether a subject has non-Hodgkins lymphoma comprising:

(a) incubating a sample of suitable body fluid from the subject with [a monoclonal antibody reactive with non-Hodgkin's lymphoma cells] an antibody that binds to a polypeptide having the sequence set forth in SEQ ID NO:2, [which] wherein the antibody is bound to a solid support;

(b) [removing unbound cells] separating the sample from the support, and

(c) determining [the presence of non-Hodgkins lymphoma cells bound to the support] whether the polypeptide is bound to the antibody, [such presence indicating that] the presence of the polypeptide indicating that the subject has non-Hodgkins lymphoma.

43771-AZY-PCT-US/JPW/AJM/APE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Riccardo Dalla-Favera and Raju S.K. Chaganti

Serial No.: 09/761,117

Filed : January 16, 2001

For : CLONING AND USES OF THE GENETIC LOCUS bcl-6

1185 Avenue of the Americas
New York, New York 10036
April 4, 2001

Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

SUPPLEMENTAL AMENDMENT

This Amendment is submitted in order to supplement the Preliminary Amendment submitted along with the above-identified application.

Please amend the above-identified application as follows:

In the claims:

Please add new claims 46-53 as follows:

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46. (New) An assay for determining whether a subject has non-Hodgkin's lymphoma, comprising (a) incubating a sample of suitable body fluid from the subject with a monoclonal antibody reactive with non-Hodgkin's lymphoma cells, which antibody is bound to a solid support, (b) removing unbound cells from the support, and (c) determining the presence of non-Hodgkin's lymphoma cells bound to the support, such presence indicating that the subject has non-Hodgkin's lymphoma.

C'

47. (New) A method for determining whether an agent is useful for treating non-Hodgkin's lymphoma, which comprises (a) determining the amount of nucleic acid having the sequence set forth in SEQ. ID NO:1 present in a suitable sample from a subject afflicted with non-Hodgkin's lymphoma, (b) administering to the subject a suitable amount of the agent under suitable conditions, (c) after a suitable period of time, again determining the amount of nucleic acid having the sequence set forth in SEQ. ID NO:1 present in a suitable sample from the subject, a difference between the nucleic acid amounts determined in steps (a) and (c) indicating that the agent is useful for treating non-Hodgkin's lymphoma.

C' cont.

48. (New) A method for determining whether a subject is afflicted with B-cell lymphoma comprising:

(a) obtaining a DNA sample from the subject;

(b) cleaving the DNA in the sample into fragments;

(c) separating the DNA fragments by size fractionation;

(d) hybridizing the separated DNA fragments with a nucleic acid molecule comprising a region of at least 15 nucleotides capable of specifically hybridizing with the nucleic acid sequence of the bcl-6 locus, so as to detect the DNA fragment containing the bcl-6 sequence; and

(e) comparing the DNA fragment detected in step (d) with the corresponding DNA fragment from a subject known not to be afflicted with B-cell lymphoma, a difference in size between these fragments indicating that the subject is afflicted with B-cell lymphoma.

49. (New) The method of claim 48, where in step (b), the DNA sample is cleaved into fragments by means of a restriction

enzyme.

50. (New) The method of claim 48, wherein the size fractionation in step (c) is performed by means of a polyacrylamide or agarose gel.

51. (New) The method of claim 48, wherein in step (d), the nucleic acid molecule is labeled with a detectable marker.

52. (New) The method of claim 51, wherein the detectable marker is a radio-labeled molecule, a fluorescent molecule, an enzyme, or a ligand.

C'
cont.

53. (New) The method of claim 48, further comprising transferring the DNA fragments from step (c) onto a solid matrix prior to step (d).

54. (New) A method of treating a subject afflicted with non-Hodgkin's lymphoma, comprising administering to the subject's lymphoma cells an effective amount of an antisense molecule capable of hybridizing to the nucleic acid molecule having the sequence set forth in SEQ. ID NO:1, thereby treating the subject.

55. (New) A method of treating a subject afflicted with non-Hodgkin's lymphoma, comprising administering to the subject's lymphoma cells an effective amount of an antagonist capable of blocking the expression of the polypeptide having the amino acid sequence set forth in SEQ. ID NO:2, thereby treating the subject.

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WASHINGTON, D.C. 20231
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BIBDATASHEET

Bib Data Sheet

CONFIRMATION NO. 3093

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
09/761,117	01/16/2001 RULE	530	1647	43771-A-PCT-US-Y/JPW/EMW

APPLICANTS

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Riccardo Dalla-Favera, New York, NY;

** CONTINUING DATA **********
THIS APPLICATION IS A DIV OF 09/268,202 03/15/1999 PAT 6,174,997
WHICH IS A DIV OF 08/553,541 05/28/1996 PAT 5,882,858
WHICH IS A CON OF PCT/US94/06669 06/09/1994
WHICH IS A CIP OF 08/074,967 06/09/1993 PAT 5,641,672

** FOREIGN APPLICATIONS **********

IF REQUIRED, FOREIGN FILING LICENSE GRANTED ** SMALL ENTITY **
** 04/09/2001

Foreign Priority claimed / 35 USC 119 (a-d) conditions met / Verified and Acknowledged	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☐ yes ☐ no ☐ yes ☐ no ☐ Met after Allowance Examiner's Signature Initials	NY	23	10	1

ADDRESS
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TITLE
Cloning and uses of the genetic locus bcl-6

FILING FEE RECEIVED 355	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit